

**REMARKS**

Claims 1-15, 17-33, 35-39 and 41-42 were pending in the application. Claims 2, 5, 7-8, 22, 24, 27 and 41-42 are withdrawn from consideration. However, as discussed below, Applicants respectfully request that the Examiner reconsider claims 2, 5, 7-8, 22, 24, 27 and 41-42 in light of the amendment presented herein. Further, claims 1-2, 5-8, 14, 23-24, 26-28 and 32 have been amended and new claims 43 and 44 have been added. Accordingly, upon entry of the instant response, claims 1-15, 17-33, 35-39 and 41-44 will remain pending in the application.

Support for the amendments to the claims can be found throughout the specification and the claims as originally filed. Specifically, support for the amendment to claims and 1 and 23 is present, at least, for example, at page 2, lines 23-25; page 4, lines 10-13; page 27, line 7 through page 8, line 23; and page 36, lines 27-32 of the specification. Support for the amendment to claim 2 and new claims 43 and 44 is present, at least, for example, at page 2, lines 26-31; page 4, line 13-16; page 5, line 10-13; page 6, lines 29-30; page 19, lines 4-11.

*No new matter has been added.* The foregoing claim amendments should in no way be construed as an acquiescence to any of the Examiner's rejections and were made solely in the interest of expediting prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

***Acknowledgment of the Examiner's Withdrawal of Certain Rejections and Objections***

Applicants gratefully acknowledge the Examiner's withdrawal of the previous rejection of claims 1, 4, 9-10, 12-13, 15, 20-21, 23, 26, 29-31, 33 and 38-40 as being anticipated by Foster *et al.* (U.S. Patent 5,217,954).

***Claim Objections for Minor Informalities***

The Examiner has maintained the objection to claims 1, 3, 4, 9-13, 15, 17-21, 23 and 28 as reading on non-elected species. The Examiner asserts that Applicants must amend the claims to delete reference to the non-elected species.

Applicants respectfully traverse this objection. As provided in M.P.E.P. § 809.02(c) and § 821, the election of a species is for search purposes only and does not necessitate that Applicants cancel or amend the claims so that they no longer read on non-elected species. Rather the claims are held as withdrawn and upon the allowance of a generic or linking claim,

Applicants are entitled to a search of additional species. As such, an amendment of the claims to remove the non-elected subject matter is not required at the present time.

Notwithstanding the above, Applicants have amended the claims (including the withdrawn claims) to specify compositions comprising a protein formulated with DTPA and **DEF** (and, optionally, mannitol, methionine or histidine) or a protein formulated with EGTA and **DEF** (and, optionally, mannitol, methionine or histidine) (and methods thereof). Accordingly, as the claims are now all drawn to the elected species of DEF, Applicant respectfully requests that the Examiner rejoin the withdrawn claims and examine claims 1-15, 17-33, 35-39 and 41-44 based on the amendments presented herein.

***Rejection of Claims 1, 4, 9-10, 12-13, 15, 17-21, 23, 26, 29-31, 33 and 35-39  
Under 35 U.S.C. § 103***

Claims 1, 4, 9-10, 12-13, 15, 17-21, 23, 26, 29-31, 33 and 35-39 are rejected as being unpatentable over Foster *et al.* (U.S. Patent 5,217,954) in view of Hagiwara *et al.* (U.S. Patent No. 6,165,467). The Examiner relies on Foster *et al.* for teaching the use of a pharmaceutical formulation comprising a protein, bFGF, a stabilizing chelator, such as DTPA or EGTA to protect bFGF from oxidation. The Examiner further relies on Foster *et al.* for teaching an agent for tonicity, a preservative or other auxiliaries, such as mannitol, glycerol, sodium chloride or Tris.

Although the Examiner acknowledges that Foster *et al.* do not teach preparing a formulation comprising an antibody, the Examiner alleges that Hagiwara *et al.* cures this deficiency. Specifically, the Examiner relies on Hagiwara *et al.* as teaching a stable human monoclonal antibody preparation and that human monoclonal antibodies have the undesirable property of aggregating and precipitating in a solution state. As such, the Examiner concludes that it would have been obvious to one of ordinary skill in the art to prepare a composition comprising a human monoclonal antibody instead of FGF according to the methods taught by Foster *et al.*

Applicants respectfully traverse this rejection. However, to expedite prosecution and allowance of the pending claims, Applicants have amended claims 1-2, 5-8, 14, 23-24 and 26-28 to specify compositions comprising a protein formulated with **DTPA and DEF** (and, optionally, mannitol, methionine or histidine) or a protein formulated with **EGTA and DEF** (and, optionally, mannitol, methionine or histidine) (and methods thereof), which are neither neither

taught nor suggested by the cited references. In fact, neither reference even mentions DEF (deferroxamine). As taught in Applicants' specification, Applicants were the first to discover the unexpected and surprising synergistic effect that the combination of DTPA and DEF has on reducing/preventing protein oxidation (see, for example, page 2, lines 23-25; page 4, lines 10-13; page 27, line 7 through page 8, line 23; and page 36, lines 27-32 of the specification).

Applicants were also the first to discover that the combination of EGTA and DEF confers a protective effect (see, for example, page 2, lines 24-25, page 4, lines 6-10; page 14, lines 4-7; page 28, lines 26 through page 29, line 10 of the specification). Only by way of Applicants' inventive contribution did Applicants successfully arrive at the claimed compositions and methods, which stabilize and protect proteins against oxidative degradation. Based at least on the foregoing, the pending claims are patentable. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection.

***Rejection of Claims 1, 3-4, 6, 9-15, 21, 23, 25-26, 28-33 and 39 Under 35 U.S.C. § 103***

Claims 1, 3-4, 6, 9-15, 21, 23, 25-26, 28-33 and 39 are rejected as being unpatentable over Kerwin *et al.* (U.S. Patent 5,929,031) in view of Hagiwara *et al.* (U.S. Patent No. 6,165,467). The Examiner relies on Kerwin *et al.* as teaching the preparation of a pharmaceutical composition which comprises hemoglobin, a reducing agent, chelators (such as DTPA and/or EGTA) and mannitol.

While the Examiner acknowledges that Kerwin *et al.* do not teach preparing a formulation comprising an antibody, the Examiner alleges that Hagiwara *et al.* cures this deficiency. Specifically, the Examiner relies on Hagiwara *et al.* as teaching a stable human monoclonal antibody preparation and that human monoclonal antibodies have the undesirable property of aggregating and precipitating in a solution state. As such, the Examiner concludes that it would have been obvious to one of ordinary skill in the art to prepare a composition comprising a human monoclonal antibody instead of hemoglobin according to the methods taught by Kerwin *et al.*

Applicants respectfully traverse this rejection. The claims, as amended, are drawn to compositions comprising a protein formulated with ***DTPA and DEF*** (and, optionally, mannitol, methionine or histidine) or a protein formulated with ***EGTA and DEF*** (and, optionally, mannitol, methionine or histidine) (and methods thereof), which are neither taught nor

suggested by the cited references. In fact, neither reference even mentions DEF (deferoxamine). As discussed in detail above, Applicants were the first to discover the unexpected and surprising synergistic effect that the combination of DTPA and DEF has on reducing/preventing protein oxidation. Applicants were also the first to discover that the combination of EGTA and DEF confers a protective effect. Only by way of Applicants' inventive contribution did Applicants successfully arrive at the claimed compositions and methods which stabilize and protect proteins against oxidative degradation.

Based at least on the foregoing, the pending claims are patentable. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection.

### **CONCLUSION**

In view of the above amendments and remarks set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney could be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

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Respectfully submitted,

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